

Amendments to the Specification

Please replace the paragraph beginning at page 2, line 6 with the following amended paragraph.

EpoR cDNA has been isolated recently from mouse liver, Tojo et al., *Biochem. Biophys. Res. Comm.* 148: 443-48 (1987) and from human fetal liver. Jones et al., *Blood* 76:31-35 (1990); Winkelmann et al., *Blood* 76:24-30 (1990). The full length EpoR cDNA sequence reported in Winkelmann is shown in the Sequence Listing as SEQ ID NO: 4. The EpoR cDNA sequence reported in Jones et al. is SEQ ID NO:6. The human cDNA encodes a polypeptide chain of MW about 55 kDa and having about 508 amino acids. The polypeptide encoded by the Winkelmann cDNA is SEQ ID NO:5. The polypeptide encoded by the Jones et al. cDNA is SEQ ID NO:7. The two polypeptide sequences differ at amino acid residues 102, 189, 190, and 244. Genomic clones of human EpoR have been isolated and sequenced. Penny and Forget, *Genomics* 11:974-80 (1991); Noguchi et al., *Blood* 78:2548-2556 (1991). Analysis of the coding sequence predicts about 24 amino acid residues in a signal peptide, about 226 amino acids in an extracellular domain, about 23 amino acids in a membrane-spanning domain, and about 235 amino acids in a cytoplasmic domain. D'Andrea and Zon, *J. Clin. Invest.* 86:681-687 (1990); Jones et al., *Blood* 76:31-35, (1990); Penny and Forget, *Genomics* 11: 974-80 (1991). The mature human EpoR protein has about 484 amino acids. All human erythroid progenitor cells have been shown to contain Epo receptors. Binding of Epo appears to decline as erythroid progenitor cells mature, until Epo receptors are not detectable on reticulocytes. Sawada et al., *J. Clin. Invest.* 80:357-366 (1987). Sawada et al., *J. Cell. Physiol.* 137:337 (1988). Epo maintains the cellular viability of the erythroid progenitor cells and allows them to proceed with mitosis and differentiation. Two major erythroid progenitors responsive to Epo are the Burst-forming units-erythroid (BFU-E) and the Colony-forming units-erythroid (CFU-E). The Epo receptor number correlates very well with the response to Epo in normal BFU-E and CFU-E. Epo receptor numbers appear to decline after reaching the peak receptor number at the CFU-E stage in human and murine cells. Sawada et al., *J. Clin. Invest.* 80:357-366 (1987); Landschulz et al., *Blood* 73:1476-1486 (1989). The recovery of Epo receptors after removal of Epo appears to be dependent on protein synthesis, which suggests downregulation of Epo receptor by

degradation, and the subsequent upregulation of receptors by the new synthesis of receptors when Epo is removed. Sawyer and Hankins, *Blood* 72:132 (1988). Studies of Epo receptors on megakaryocytes and erythroid progenitors suggest that there is a link between the regulation of erythropoiesis and thrombopoiesis, in that stimulation of cell division by both cell types is controlled by Epo receptor numbers. Berridge et al., *Blood* 72:970-977 (1988). Although the Epo receptor has been cloned, the precise mechanisms involved in binding of Epo to Epo receptors and the relationship to subsequent erythropoietic processes are not known.

Please replace the paragraph beginning at page 14, line 10 with the following amended paragraph.

PCR amplification was carried out using a full-length human EpoR cDNA, LAP37, SEQ ID NO:4, as a template. The 5'-sense primer (SEQ ID NO:1) was 5'-TTGGATCCGCGCCCCGCCTAAC-3'. This primer has a BamH1 linker sequence at the 5' end, followed by the coding sequence for amino acids 25 through 29 of the full length human EpoR protein. The 3'-antisense primer (SEQ ID NO:2) was 5'-TGAATTGGGTCCAGGTCGCT-3'. This primer has an EcoR1 linker followed by sequence complementary to the coding sequence for amino acids 250 through 246 of full length EpoR. Using a Perkin Elmer-Cetus PCR kit, PCR was carried out with 0.1 µg of LAP37 (SEQ ID NO:4) cDNA, 20 pM of each primer, 1.25 mM dNTP mixture (dGTP, dCTP, dTTP and dATP), 0.5 µl of Taq polymerase, and 10x buffer supplied in the PCR kit. Amplification was carried out by a PTC-100 Programmable Thermal Controller, (M.J. Research, Inc. Watertown, Mass.), with denaturation at 94°C for 1 min, annealing at 55°C for 1 min and extension at 72°C for 1 1/2 min, repeated for 25 cycles.

Please add SEQ ID NO:5, SEQ ID NO:6, and SEQ ID NO:7 to the application after the specification and before the claims. SEQ ID NOS:5-7 are enclosed herewith in paper form and as a floppy disc.